EXHIBIT A

Dkt. # 702-A-US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Schwartz et al.
U.S. Serial No.	:	10/693,301
Confirmation No.	:	1477
Filed	:	October 24, 2003
Examiner	:	Paul C. Martin
Art Unit	:	1655
For	:	SCREENING, QUANTITATION AND IDENTIFICATION OF ACTIVE INGREDIENTS IN NATURAL PRODUCTS

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

DECLARATION UNDER 37 C.F.R. §1.132

1. I, Gary K. Schwartz, hereby declare that I am the Chief of the newly created Melanoma and Sarcoma Service in the Department of Medicine's Division of Solid Tumor Oncology at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York. I am a physician-scientist who specializes in the identification and development of new targeted drugs for cancer therapy, particularly in the treatment of patients with gastrointestinal cancers and sarcomas. These agents are not disease specific and hold promise in the treatment of all solid tumor malignancies. My research studies have been supported by the National Cancer Institute, the Lustgarten Foundation for Pancreatic Cancer, the Department of Defense for Breast Cancer Research, the Byrne Foundation, the Food and Drug

Administration, and the generous philanthropic support of MSKCC patients and their families. A copy of my resume is enclosed herein as Exhibit 1.

2. I am also a co-inventor of U.S. Patent Application No. 10/693,301, filed October 24, 2003, and I am familiar with the subject matter of the above-referenced patent application, which is drawn to a method for treating cancer in a subject comprising administering to the subject a composition of aqueous coptis chinesis extract.

3. In a non-final Office Action mailed September 26, 2006, the Examiner to whom the above-referenced application was assigned rejected the application under 35 U.S.C. 103(a) as being unpatentable over Li et al. (Mol. Pharmacol. 58:1287-1293 (2000)). The Examiner contends that Li et al. teach a method of inhibiting cancer cell growth by administering an effective amount of aqueous chinesis extract. The Examiner also contends that Li et al. teach 100% tumor growth inhibition can only be achieved using the whole herbal extract (*see* page 4 of the Office Action).

4. Accordingly, the Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to have used the method of Li et al. for inhibiting cell growth in human cancer cells by administering an effective amount of aqueous chinesis extract as a treatment of a solid tumor in a subject because the herbal extract was shown to inhibit cancer cell growth *in vitro*. The Examiner contends that there would have been a reasonable expectation of success in adapting the method of Li et al. to treat cancer in a subject (*see* page 5 of the Office Action).

5. Li et al. only show cancer cell growth inhibition *in vitro*. Li et al. did not provide any data with regard to using aqueous chinesis extract *in vivo*. I hereby declare that the *in vitro* data of Li et al. do not provide one of ordinary skill in the art a reasonable expectation of success in using aqueous chinesis extract to treat cancer in a subject. It is well recognized in the art that *in vitro* data, even promising ones, do not necessarily lead to successful uses in clinics. *In vitro* data provide at best minimal, if not irrelevant,

guidance on whether the drug in question will have clinical efficacy. In other words, whether a drug or composition will be useful in clinic can only be determined by vigorous clinical trials. For example, Flavopiridol, an inhibitor of several cyclin-dependent kinases, exhibited potent growth-inhibitory activity against prostate cancer cells *in vitro* (Li et al., *Int. J. Oncol.* 17:755-759 (2000)). A copy of Li (2000) is attached hereto as Exhibit 2. However, results from clinical trial indicated that Flavopiridol was ineffective in patients with previously untreated metastatic hormone-refractory prostate cancer (Liu et al., *Clinical Cancer Research* 10:924-928 (2004)). A copy of Liu (2004) is attached hereto as Exhibit 3. Another example is endostatin, the famous angiogenesis inhibitor that inhibited endothelial cell proliferation *in vitro*, and even caused primary tumor regression in animal model (O'Reilly et al., *Cell* 88:277–285 (1997)). A copy of O'Reilly (1997) is attached hereto as Exhibit 4. However, results from a Phase I clinical trial with patients having refractory solid tumors indicated that no clinical response was generated by using endostatin, even though endostatin was well tolerated (Thomas et al., *J. Clinical Oncol.* 21:223-231 (2003)). A copy of Thomas is attached hereto as Exhibit 5. Similarly, endostatin also failed in a Phase II clinical trial with patients having advanced neuroendocrine tumors (Kulke et al., *J. Clinical Oncol.* 24:3555-3561 (2006)). A copy of Kulke (2006) is attached hereto as Exhibit 6. Hence, in view of the above remarks and knowledge generally available in the art, I hereby conclude that relying on Li's *in vitro* data alone, there would not have been a reasonable expectation of success in adapting the method of Li et al. to treat cancer in a subject.

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6. I hereby declare that all statements made of my own knowledge are true and that all statements made on information and belief are believed to be true. I acknowledge that making willful false statements and the like are punishable by fine or imprisonment, or both (18 U.S.C. 1001), and may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,

Gary K Schwartz 11/24/06

Dr. Gary K. Schwartz Date